In vitro study of the effect of ZD1839 on glioblastoma tumor cells

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BACKGROUND AND OBJECTIVES. ZD1839 is a selective and potent inhibitor of the tyrosine kinase associated with the epidermal growth factor receptor (EGFR). Its clinical efficacy has been demonstrated for several malignancies. As EGFR has also been reported to be expressed in some glioblastoma (GBM) tumor cells, we studied the effect of ZD1839 on the viability and growth capacity of glioblastoma tumor cells in vitro.
METHODS. Cells from the GBM cell lines U251, T98G, A172, or freshly isolated GBM cells from a patient or fibroblasts were cultured during 1, 2, 3 or 6 days in the presence of different concentrations of ZD1839. At the end of the culture, the viability of the remaining GBM cells was analyzed with the MTT assay. In other experiments, GBM cells were washed after 24 hours culture in the presence of ZD1839, and were further cultured for 5 days in the absence of ZD1839, before viability was analyzed.
RESULTS. Addition of different concentrations of ZD1839 for 1 or 2 days had no effect on the viability and growth of the GBM cells. Prolonged exposure of GBM cells to higher concentrations of ZD1839 (10 uM) resulted in a small reduction of the in vitro expansion of the GBM cells as compared to the control cultures.
CONCLUSION. Using in vitro culture systems of cell lines and freshly isolated GBM cells of unknown EGFR status, we could not demonstrate a direct cytotoxic of cytostatic effect of ZD1839 on cell viability or growth, except under conditions of prolonged exposure at supraphysiological concentrations. However, anti-angiogenic activity could not be evaluated suggesting further investigation in in vivo glioblastoma models. Further studies should also assess EGFR expression/drive in GBM cells.